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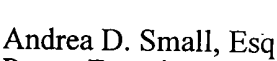
IT 82552-65-6P, 1,2-Bis(aziridin-N-yl)glyoxime
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for prepn. of nickel(II), palladium(II) and cobalt(II) bis(aziridinyl)glyoximato complexes)

RN 82552-65-6 CAPLUS
CN Aziridine, 1,1'-[1,2-bis(hydroxyimino)-1,2-ethanediyl]bis- (9CI) (CA INDEX NAME)



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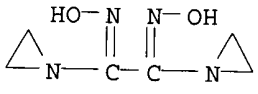

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Contents

J. Chem. Research (S), 1999, 142–143†

Synthesis and Characterization of 1,2-Bis(aziridin-*N*-yl)glyoxime and its Nickel(II), Palladium(II) and Cobalt(II) Complexes†‡

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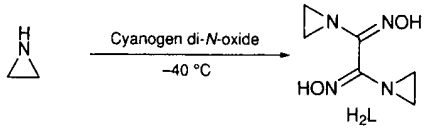
An aziridine functional *vic*-dioxime ligand and complexes with Ni^{II}, Pd^{II} and Co^{II} are prepared starting from aziridine by the reaction of cyanogen di-*N*-oxide.

Vicinal dioximes have received considerable attention as model compounds for vitamin B_{12} and their complexes have been the source, through the decades, of a never-ending series of interesting reports. The exceptional stability of these complexes can be attributed to their planar structure which is stabilized by hydrogen-bonded bridges. Our group has initiated a series of studies on the chemistry of transition metal complexes of *vic*-dioximes incorporating cyclopentadienyl groups,[1] amino-crown ether,[2] thia-crown ether,[3] tetrathia macrocycles,[4] alkylthia ether groups,[5] monoaza and benzomonoaza[6] diazadioxa[7] quinoxalinyl groups,[8] and dendritic groups.[9]

The consequences of these functional groups are to effect the physical properties, *e.g.* solubility, melting point, gas sensing[10] and phase transfer catalysis[3].

The reaction of amines or thiols with (*E*,*E*)-dichloroglyoxime or cyanogen di-*N*-oxide yielded various symmetrically substituted diaminoglyoxime or dithioglyoxime derivatives.[11] The (*E*,*E*)- and (*E*,*Z*)-stereoisomers of vicinal dioximes are capable of coordinating through N,N or N,O sites of the oxime groups. In the case of (*E*,*E*)-monochloroglyoxime, asymmetric vicinal dioximes have been obtained. Transition metal complexes of these vicinal dioximes are essentially *N*,*N*-coordinated square-planar structures. Now, we report on a vicinal-dioxime ligand in which these donor groups are directly bound to the N-pivot atoms of two aziridine units and its complexes with Ni^{II}, Pd^{II} and Co^{II}. Here aziridine groups have been chosen owing to their effectiveness in the field of carcinogenic activity.

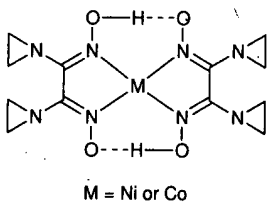
Some of the aziridine derivatives exhibit anticarcinogenic activity, and hence, find use as antitumor agents. *o*-Ethoxyphenyl-*N*-carbamoylaziridine shows anticarcinogenic activity as shown using the pulmonary tumor-induction method in Strain A mice. Aziridines as a class are more active than the carbamates, with 3,4-dichlorophenyl-*N*-carbamoylaziridine being over 20 times more active on a molar dose basis than ethyl carbamate, which is the most active of the carbamates.[12] *N*,*N*′-Octamethylene-bis-1-azirdine acetamide was effective in reducing the presence of carcinoma cells in the lung.[13] A Raman investigation of hexaziridinocyclo triphosphazene interactions with DNA *in vitro* suggests that the alkylating sites on DNA for this powerful antitumor agent are the N(7) and NH_2 positions of adenine.[14] A survey of crystal structures for aziridinocyclophosphazenes shows that antitumor activity is presumably related to some specific 'bow-tie' conformation of aziridine wings which may be present in active drugs, rather than to the number of aziridine groups in the molecule.[15] Many aziridinocyclophosphazenes exhibit antitumor activity and this behaviour is attributed to the alkylating ability of these compounds by the facile opening of aziridine rings.[16]



Scheme 1

1,2-bis(aziridin-*N*-yl)glyoxime (H_2L) was synthesized from aziridine and cyanogen di-*N*-oxide (Scheme 1). The product was obtained by treating a suspension of (*E*,*E*)-dichloroglyoxime in dichloromethane with 1 M aq. Na_2CO_3 at −40 °C.[17] and elemental analysis of the white crystal line material corresponds to $C_6H_{10}N_4O_2$. A symmetrical *s*-trans form is expected for H_2L. In the IR spectrum of H_2L, the OH, C=N and N–O stretching vibrations are observed at 3200, 1620 and 950 cm^{-1} respectively, in agreement with values reported for similar compounds.[2,17] The ^1H NMR spectrum in $(CD_3)_2SO$ exhibits a D_2O exchangeable signal for OH (δ 10.40) and a singlet for the CH_2 groups (δ 2.09). More detailed information about the structure of H_2L was provided by ^{13}C NMR spectroscopy. The carbon resonance of the carbohydroximamide moiety was found at δ 151.24 and the CH_2 groups attached to the N-atom was observed at δ 28.17. The EI mass spectrum of H_2L shows the molecular ion peak at $m/z = 170$. H_2L was soluble in ethanol, Me_2SO, hot MeCN and DMF, but insoluble in dichloromethane, chloroform, acetone and diethyl ether.

To prepare complexes of H_2L with Ni^{II}, Pd^{II} and Co^{II} a solution of the ligand and a metal salt in EtOH was heated to 55–60 °C while an equivalent amount of NaOH in EtOH was added gradually. The IR spectra of the complexes are very similar to those of H_2L, except for the disappearance of the OH stretching frequencies for the Ni^{II} complex (Fig. 1). Weak bands at *ca.* 1700–1710 cm^{-1} indicated O–H···O hydrogen-bonded bridges while the C=N vibrations appeared at lower wavenumbers,[2,6] as expected for *N*,*N*-chelated vicinal-dioxime complexes. The diamagnetic nature of the nickel(II) and palladium(II) complexes were confirmed by their ^1H NMR spectra. The reddish color of $Ni(HL)_2$ is in accord with that of previously reported *vic*-dioximate complexes.[18]



M = Ni or Co

Fig. 1 The structure of $[M(HL)_2]$

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.
‡Dedicated to Professor Dr. Özer Bekaroğlu on the occasion of his 65th birthday (May 3, 1998) with our best wishes.

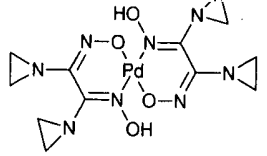

Fig. 2 The structure of $[Pd(HL)_2]$

In the ^1H NMR spectrum of $Ni(HL)_2$ the deuterium exchangeable O–H···O protons were observed at δ 17.2 as a singlet and CH_2 protons were observed at δ 3.29–3.61 as a multiplet. For the Pd^{II} complex the IR spectrum shows that the OH vibration is still present in the molecule (3200 cm^{-1}) and the OH proton was observed at δ 12.24 and CH_2 protons at δ 3.25–3.81 as a multiplet in the ^1H NMR spectrum. This type of coordination is more usual in (*E,Z*)-complexes, were the ligand forms a six-membered chelate ring by coordinating to Pd through the N and O atoms as shown in Fig. 2. Attempts to record ^{13}C NMR spectra of these complexes were unsuccessful due to their low solubility. The structures of $Ni(HL)_2$ and $Pd(HL)_2$ are also confirmed by mass spectroscopy, which give a $[M-1]^+$ peak at *m/z* 396 and $[M+1]^+$ peak at *m/z* 446 respectively. Owing to the insolubility of the cobalt(II) complex, its mass spectrum could not be obtained.

Experimental

Routine IR spectra were recorded on a Perkin-Elmer 983 spectrophotometer as KBr pellets. Elemental analysis were performed using a Carlo Erba 1106 Instrument. ^1H and ^{13}C NMR spectra were recorded on a Bruker 200 MHz spectrometer. Mass spectra were recorded on a VG Zabspec GC-MS spectrometer with electron impact methods.

Aziridine was synthesized according to the reported procedure.[19] For the first time, the synthesis of aziridino dioximes, isomerization, and their reaction to obtain oxadiazines were achieved by Eremeev *et al.*[20]

Synthesis of 1,2-*Bis*(*aziridin-N-yl*)*glyoxime* (H_2L).—To a stirring solution of aziridine (0.762 g, 17.7 mmol) in 300 ml of CH_2Cl_2 a solution of cyanogen di-*N*-oxide in CH_2Cl_2 (200 ml) was added at −40 °C which was obtained by treating a suspension of dichloroglyoxime (2.03 g, 13 mmol) with 300 ml of 1 M Na_2CO_3. The reaction mixture was stirred at −40 °C for 2 h, then allowed to warm to room temperature. The product was filtered off and washed with dichloromethane. Recrystallization from EtOH (100 ml) gave the pure product. Yield: 0.4 g (27%). mp 192–195 °C (decomp) (Found; C, 42.17; H, 5.67; N, 32.27. $C_6H_{10}N_4O_2$ requires C, 42.35; H, 5.92; N, 32.92%). ν_{max}/cm^{-1} 3200 (OH), 2860 (CH_2), 1620 (C=N), 1450, 1380, 1305, 1160, 1080, 1010, 950 (N–O), 900, 800, 750, 700; δ_H [$(CD_3)_2SO$] 10.4 (s, 2 H, NOH, disappeared upon D_2O exchange), 2.09 (s, 8 H, CH_2N); δ_C [$(CD_3)_2SO$] 151.24 (C=NOH), 28.17 (CH_2N); *m/z* (100%, M^+), 123(17), 112(100), 95(74), 85(53), 82(30), 69(81), 67(55), 56(40).

Ni(*HL*)$_2$.—To a solution of 0.2 g (1.176 mmol) of H_2L in 25 ml of hot ethanol (60 °C) was added, $NiCl_2 \cdot 6H_2O$ (0.14 g, 0.588 mmol) in 10 ml of ethanol. A decrease in pH was observed and the yellowish-orange nickel(II) complex precipitated. The mixture was then heated to 60 °C for 15 min and an equivalent amount of NaOH (0.1 M in EtOH) was added dropwise to maintain a pH value of 5.5. The reaction mixture was then cooled to room temperature and the product filtered off, washed with EtOH, water, hot EtOH and dried with diethyl ether. Yield: 0.067 g (29%). m.p. >270 °C (Found; C, 36.08; H, 4.53; N, 28.4. $C_{12}H_{18}N_8NiO_4$ requires C; 36.3; H, 4.57; N, 28.22%); ν_{max}/cm^{-1} 2860, 2820 (CH_2), 1705 (O–H···O), 1600 (C=N), 1310, 1040, 940 (N–O), 880; δ_H [$(CD_3)_2SO$] 17.19 (s, 2 H, O–H···O, disappeared by D_2O exchange), 3.11–3.52 (m, 16 H, CH_2N); *m/z* 396 (15%, $[M-1]^+$), 207(16), 170(52), 154(15), 136(43), 105(54), 91(100), 73(69), 59(54).

Pd(*HL*)$_2$.—$Pd(HL)_2$ was prepared according to the same procedure as described for the preparation of $Ni(HL)_2$ by starting from H_2L (0.2 g, 1.176 mmol). Na_2PdCl_4 [prepared by stirring 0.104 g (0.588 mmol) of $PdCl_2$ and 0.069 g (1.176 mmol) of NaCl in 20 ml of EtOH] was used. A dark-orange palladium(II) complex was obtained. Yield: 0.074 g (28.3%); m.p. >270 °C (Found; C, 32.07; H, 3.77; N, 24.66. $C_{12}H_{18}N_8O_4Pd$ requires C, 32.41; H, 4.08; N, 25.2%); ν_{max}/cm^{-1} 3200 (OH), 2860, 2820 (CH_2), 1590 (C=N), 1440, 1340, 1040, 940 (N–O), 880; δ_H [$(CD_3)_2SO$] 12.24 (s, 2 H, OH, disappeared by D_2O exchange), 3.25–3.52 (m, 16 H, CH_2N); *m/z* 446 (41%, $[M+1]^+$), 396(7), 354(42), 279(100), 256(41), 242(13).

Co(*HL*)$_2$.—$Co(HL)_2$ was prepared according to the same procedure as described for the preparation of Ni)$HL)_2$ by starting from H_2L (0.15 g, 1.026 mmol). $CoCl_2 \cdot 6H_2O$ (0.122 g, 0.513 mmol) was used and a brown cobalt(II) complex was obtained. Yield: 0.127 g (62.4%); mp >270 °C (Found; C, 35.97; H, 4.31; N, 27.89; $C_{12}H_{18}CoN_8O_4$ requires C, 36.28; H, 4.56; N, 28.2%); ν_{max}/cm^{-1} 2860, 2820 (CH_2), 1705 (O–H···O), 1600 (C=N), 1440, 1320, 1040, 940 (N–O), 850.

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